

### Evidence for the agricultural origin of antimicrobial resistance in a fungal pathogen of humans

S. Earl Kang, Leilani G. Sumabat, Tina Melie, Brandon Mangum, © Michelle Momany, © Marin T. Brewer doi: https://doi.org/10.1101/2020.05.24.113787

- Showed that azole-resistant isolates of A. fumigatus from clinical and agricultural settings also carry
  mutations conferring resistance to quinone outside inhibitor (QoI) fungicides, which are used
  exclusively in agricultural settings.
- Fourteen (8 agricultural, 6 from patients) of 19 pan-azole-resistant A fumigatus isolates included in the study also carried mutations for QoI resistance
- This is the first report of a clear marker for the agricultural origin of resistance to a clinical antifungal.

PLOS pathogens

#### Azole-resistant *Aspergillus fumigatus* in the environment: Identifying key reservoirs and hotspots of antifungal resistance

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- · Literature review: the global occurrence of azole-resistant A. fumigatus in the environment; interactive world map showing where resistant isolates have been detected and includes information on the specific alleles identified, environmental settings, and azole fungicide use
- Developed environments, specifically hospitals and gardens, were the most common settings where azole-resistant A. fumigatus was detected, followed by soils sampled from agricultural settings (~37%). Sampling/reporting bias is likely a factor
- TR<sub>34</sub>/L98H resistance allele was the most common in all regions except South America where the  $TR_{46}/Y121F/T289A$  allele was the most common.
- Call for increased surveillance to pinpoint reservoirs, need for antifungal stewardship to protect use of antifungals to protect both humans and crops

## Genomic Diversity of Azole-Resistant *Aspergillus fumigatus* in the United States

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- Used whole-genome single nucleotide polymorphism (SNP) analysis on 179 nationally represented clinical and environmental A. fumigatus genomes from the United States along with 18 non-U.S. genomes to evaluate the genetic diversity and foundation of the emergence of azole resistance in the United States
- Showed the presence of clades of A. fumigatus isolates: clade A (17%) comprised a global collection of clinical and environmental azole-resistant strains, including all strains with the TR<sub>32</sub>/L98H allele from India, The Netherlands, the United Kingdom, and the United States, and clade B (83%) consisted of isolates without this marker mainly from the United States.
- TR<sub>34</sub>/L98H polymorphism was shared among azole-resistant A. fumigatus strains from India, The Netherlands, the United Kingdom, and the United States, suggesting the common origin of this resistance mechanism
- Six percent of azole-resistant A. fumigatus isolates from the United States with the TR<sub>34</sub> resistance marker had a
  mixture of clade A and clade B alleles, suggestive of recombination
- Study demonstrates the genetic background for the emergence of azole resistance in the United States, supporting a single introduction and subsequent propagation, possibly through recombination of environmentally driven resistance mutations.

# Triazole resistance in human pathogen Aspergillus fumigatus on commercial plant products

Primary Category: Biology and Disease Management (Secondary Category: Mytology) (Pathogen Type Keyword: Fungus
Host Type Keyword: Other (Associated Host Type Keyword: Other (Session Type: Research On-Demand)

#### Talk at APS conference August 2021

- purpose study was to identify if azole-resistant A. fumigatus is present on commercial products in the United States
- 10 categories of retail plant products were screened for azole-resistant A. fumigatus. Of
  the approximately 500 isolates that have been collected,. 6 from peanut and compost
  have been identified as pan-azole-resistant through minimum inhibitory
  concentration (MIC) testing
- mechanism of resistance of azole-resistant isolates will be investigated by cyp51A sequencing and population genetic analyses based on STRAf genotyping will be conducted to determine the relatedness of strains collected in this study to clinical and environmental strains worldwide

- study from Japan explored genes contributing to azole tolerance in A. fumigatus by in vitro mutant selection with tebuconazole
- after three rounds of selection, obtained four isolates with low susceptibility to tebuconazole; these isolates also showed low susceptibility to itraconazole and voriconazole.